Evidence for bilateral innervation of certain homologous motoneurone pools in man

L. J. Carr, Linda M. Harrison* and J. A. Stephens

Department of Physiology, University College, Gower Street, London WC1E 6BT

1. Surface EMG recordings were made from left and right homologous muscle pairs in healthy adults. During each recording session subjects were requested to maintain a weak isometric contraction of both the left and right muscle.

2. Cross-correlation analysis of the two multiunit EMG recordings from each pair of muscles was performed. Central peaks of short duration (mean durations, 11·3–13·0 ms) were seen in correlograms constructed from multiunit EMG recordings obtained from left and right diaphragm, rectus abdominis and masseter muscles. No central peaks were seen in correlograms constructed from the multiunit EMG recordings from left and right upper limb muscles.

3. To investigate descending pathways to the homologous muscle pairs, the dominant motor cortex was stimulated using a focal magnetic brain stimulator whilst recording from homologous muscle pairs.

4. Following magnetic stimulation of the dominant motor cortex, a response was recorded from both right and left diaphragm, rectus abdominis and masseter muscles. In contrast, when recording from homologous upper limb muscles, a response was only seen contralateral to the side of stimulation.

5. The finding of short duration central peaks in the cross-correlograms constructed from multiunit recordings from left and right diaphragm, rectus abdominis and masseter, suggests that muscles such as these, that are normally co-activated, share a common drive. The mechanism is discussed and it is argued that the time course of the central correlogram peaks is consistent with the hypothesis that they could be produced by a common drive that arises from activity in last-order branched presynaptic fibres although presynaptic synchronization of last-order inputs is also likely to be involved.

6. The results of the magnetic stimulation experiments suggest that this common drive may involve the corticospinal tract.

7. We saw no evidence for a common drive to left and right homologous muscle pairs that may be voluntarily co-activated but often act independently.

Co-contraction of agonist muscles is observed during normal movements in man; the central nervous mechanisms underlying such muscle synergies, however, are still largely unknown. One possible mechanism that could account for the observed synergy is that it is due to the presence of a common drive to the motoneurone pools of the co-contracting muscles. This may be produced by activity in common stem last-order presynaptic fibres which branch and innervate the motoneurone pools of the co-contracting muscles.

To test this hypothesis, Bremner, Baker & Stephens (1991) performed cross-correlation analysis of motor unit discharges recorded simultaneously from different co-contracting finger muscles. If activity in branched last-order synaptic input is present, and/or if activity in these fibres is synchronized, then synchronization of the commonly innervated motoneurones can be expected, which will result in a short duration central peak in the cross-correlogram (Sears & Stagg, 1976). Such synchronization was found between many muscle pairs acting synergistically in the hand and forearm and the time course of the central peak of the cross-correlograms was well matched by that expected for motoneurones that receive a common innervation. Thus it was concluded that common drive via last-order branched presynaptic fibres may be the deciding factor in determining the patterns of co-contraction of these muscles and hence in characterizing a particular movement.

*To whom correspondence should be addressed.

In the present study we have tested the common innervation hypothesis further by investigating the innervation of left and right motoneurone pools supplying homologous muscle pairs in man. Motoneurones supplying left and right muscle pairs that are normally co-contracted may share a common drive; examples of such muscles are those homologous left and right muscle pairs involved in respiration, in certain movements of the trunk and in mastication. In contrast, motoneurones supplying homologous left and right muscles which can be co-contracted but normally act independently, for example left and right upper limb muscles, would not be expected to share last-order inputs.

A drive that is common to left and right motoneurone pools of homologous muscles may involve activity in the corticospinal tract. To test this hypothesis, we have studied corticospinal projections from the motor cortex using transcranial focal magnetic brain stimulation.

A preliminary account of these results has been presented to The Physiological Society (Carr *et al.* 1992).

METHOD

Subjects

Recordings were made, with local ethical approval, from twenty-one healthy adult volunteers aged 20–43 years. Subjects gave their informed consent.

Experimental procedure

Sequential recordings were made from homologous left and right muscles of the upper limb: first dorsal interosseous (FDI), forearm extensor compartment (FA Ext), biceps and deltoid muscles. Recordings were also made from the left and right diaphragm, rectus abdominis (Rectus Abd) and masseter muscles. Subjects performed a standard task to co-activate each muscle pair (Table 1). Subjects were asked to maintain a steady weak-to-moderate isometric contraction; they were aided in this by auditory and visual feedback of the EMG signal. To avoid muscle fatigue, if requested the subject was allowed to rest. When recording from the diaphragm, the integrated right diaphragmatic EMG signal was displayed on a storage oscilloscope. The subject attempted to match each inspiratory effort to the integrated display in order to achieve a regular respiratory pattern.

Data for cross-correlation analysis and from magnetic brain stimulation were collected over a number of separate recording sessions.

Electromyographic recordings

In all subjects ($n = 21$) surface EMG was recorded from left and right muscle pairs simultaneously using a two-channel EMG machine (MS6, Medelec Ltd, Old Woking, UK). Small bipolar electrodes were used for recording; these were made from neonatal ECG electrodes (Pink H82V, Arbo, Henleys Medical Supplies, Welwyn Garden City, Herts, UK), cut down to reduce their recording area to 10 by 15 mm. Electrodes were taped 5 mm apart, edge to edge, overlying the muscles under study. For the diaphragm muscle, surface electrodes were placed bilaterally over the seventh and eighth intercostal space, in the anterior axillary line. This position is estimated to be the optimal site for diaphragm recording (Lansing & Savelle, 1989; Maskill, Murphy, Mier, Owen & Guz, 1991). EMG was amplified, filtered (−3 dB at 150 Hz and 5 kHz) and stored on magnetic tape (Racal Store 4, Racal, Southampton, Hants, UK) for future analysis.

In three subjects, single and multiunit recordings were obtained from left and right masseter and in one subject from left and right rectus abdominis using monopolar concentric needle electrodes (type E/NO1; Medelec Ltd, UK). EMG was filtered at −3 dB at 2 and 5 kHz (Buller, Garnett & Stephens, 1980). Data were stored on magnetic tape (Racal Store 4) for future analysis.

ECG recording

ECGs were recorded using standard limb leads during experiments recording from left and right diaphragm. ECG data were stored together with the EMG data on magnetic tape.

Cross-correlation analysis

Diaphragm recordings. The ECG signal was removed from the recordings by using the QRS complexes from the ECG recording to produce transistor–transistor logic (TTL) pulses from a level detector (NL 200, Neurolog, Digitimer Ltd, Welwyn Garden City, Herts, UK). Each of these triggered a short circuit of the two EMG signals which had been delayed by 50 ms (NL 202, AC signal delay, Neurolog) in order to blank out signals before and after the trigger point. The duration of the short circuit was adjusted such that the entire ECG complex was removed from the EMG signal.

Cross-correlation analyses were performed as follows. Periods of silence or marked phasic EMG activity were excluded from the analysis. Medium and large amplitude spikes from each multiunit EMG signal were selected using a level detector (Neurolog NL200). The resulting trigger pulses were passed into a CED 1401 interface (Cambridge Electronic

Table 1. Tasks used to co-activate homologous muscle pairs

Muscles (left/right)	Movement
FDI	Abduct index fingers against resistance
FA Ext	Extend wrists and fingers of both hands
Biceps	Flex both elbows, holding book of *ca* 2 kg
Deltoid	Abduct both arms to 90 deg
Masseter	Clench teeth
Rectus Abd	Supine. Legs raised or trunk curl
Diaphragm	Supine. Deep voluntary respiration

Design, Cambridge, UK) for processing. Cross-correlograms were constructed with a bin width of 1 ms and a pre- and post-trigger sweep period of 100 ms. Spikes from the left muscle were arbitrarily chosen to be the trigger spikes. A minimum of 2000 spikes were used from each EMG signal. The size of any cross-correlogram peak was measured in terms of k, the peak bin count divided by the mean or baseline bin count (m), as defined by Sears & Stagg (1976). The baseline count was calculated from the first and last seventy-five bins of the cross-correlogram, a region well away from any central peak, except for diaphragm correlograms, when because of the underlying respiratory oscillation, the mean was estimated by eye as the tangent to this curve at time zero (Kirkwood, Sears, Stagg & Westgaard, 1982*b*). The criteria of Sears & Stagg (1976) were used to assess the statistical significance of any central peak.

Focal magnetic brain stimulation

Surface EMG responses evoked by focal magnetic stimulation of the motor cortex were recorded from left and right muscle pairs simultaneously. The motor cortex of the dominant hemisphere was stimulated; this was taken to be the cortex contralateral to the dominant hand (left cortex in 6 subjects and right cortex in 1 subject). A Magstim 200 stimulator (Magstim Co., Whitland, Dyfed, UK) was used with a prototype focal double-coned coil (each coil 70 mm diameter). For each muscle studied, the optimal point of stimulation was marked on the scalp. As a guide this had been previously estimated in two of the subjects using a modified 10–20 system (Jasper, 1958). Interpolar distances were measured between the external auditory meati and between nasion and inion. The scalp site over which stimulation elicited maximal responses in the contralateral muscle, was expressed as a percentage of these interpolar distances, measured from the vertex (Cz) in the coronal and sagittal planes. Table 2 gives the approximate scalp sites used for each muscle studied.

The distribution of these sites is in accord with the human motor homunculus demonstrated by Penfield & Boldrey (1937) and more recent non-invasive studies of muscle representations in the human motor cortex (Rothwell, Thompson, Day, Dick, Kachi & Cohen, 1987; Wasserman, McShane, Hallett & Cohen, 1992).

As responses could not always be evoked in relaxed muscle, the threshold of response to magnetic stimulation was established in preactivated muscle during a weak contraction. The threshold was defined as the lowest stimulus output at which a consistent reproducible response was elicited in the contralateral muscle under study. The output of the stimulator was then increased by 10 % above this value. Around five responses were recorded from preactivated muscle and where possible, five responses from relaxed muscle.

Table 2. Site of stimulation measured from Cz as a percentage of interpolar distance between (i) nasion and inion, and (ii) external auditory meati

Muscle	(i) Anterior/posterior	(ii) Lateral
Masseter	+7	23
FDI	+7	13
FA Ext	+2	13
Biceps	0	10
Diaphragm	0	10
Deltoid	−2	6
Rectus Abd	−5	3

If responses were not seen in relaxed muscle following stimulation, the output of the stimulator was increased by a further 10–20 %. Data were stored on magnetic tape. Single sweeps of EMG, time locked to the stimulus, were analysed. In addition, EMGs were full-wave rectified and averaged time locked to the stimulus (CED signal-averaging software).

In two subjects, an average of forty to sixty responses to magnetic stimulation at 10 % above threshold were analysed in the preactivated muscles of the upper limb. This was to explore any subtle alteration of ipsilateral EMG activity following stimulation.

Since the level of background EMG can affect the absolute size of the response, to enable comparison between muscles and between subjects, the area of the response was divided by the mean level of the average rectified background EMG.

RESULTS

Cross-correlation analysis

Homologous left and right muscles of the upper limb

Cross-correlograms were constructed between multiunit spike trains of left and right FDI (10 subjects); left and right FA Ext (9 subjects); left and right biceps (8 subjects); and left and right deltoid (9 subjects). All these cross-correlograms were flat; a short duration central peak was never seen in cross-correlograms constructed from multiunit EMG recordings obtained from these homologous muscle pairs. This is illustrated in Fig. 1 in which cross-correlograms from left and right FDI and left and right deltoid muscles are shown.

Homologous left and right axial and truncal muscles

In contrast to the upper limb, cross-correlograms constructed between the multiunit EMG recordings from left and right diaphragm (8 subjects), left and right rectus abdominis (8 subjects) and left and right masseter (10 subjects) showed central peaks of short duration. The strength (k) and duration of synchrony is summarized for each muscle pair in Table 3.

During deep voluntary inspiration, central peaks were found in cross-correlograms constructed between multiunit EMG recordings from left and right diaphragm in all subjects ($n = 8$). The duration of this central peak ranged from 9 to 14 ms (mean 11·3 ms) while the amplitude, expressed in terms of k ranged from 1·21 to 1·55 (mean 1·35). In all subjects this central peak was the dominant feature in the cross-correlogram, an example is shown in Fig. 2*A*. The respiratory cycle itself introduces a periodicity of around 4 s, which is reflected by the smooth decline in spike probability centred about time zero.

Marked periodicities were often observed in cross-correlograms constructed between EMG discharges of left and right diaphragm, as shown in Fig. 2*B*, in which a central peak of 10 ms duration is flanked on either side by secondary and tertiary peaks. The mean lag of the secondary peaks was 13 ms (S.D. 0·7, $n = 8$) from the central peak. This therefore reflects a periodic process with a mean value of 75 Hz (S.D. 4·5).

Table 3. Characteristics of cross-correlograms from homologous muscle pairs

Muscle Left/right	Number of subjects	Synchrony present	k	Duration (ms)
FDI	10	0/10	—	—
FA Ext	9	0/9	—	—
Biceps	8	0/8	—	—
Deltoid	8	0/8	—	—
Diaphragm	8	8/8	1·35 ± 0·14	11·3 ± 1·9
Rectus Abd	8	8/8	2·45 ± 0·73	12·1 ± 2·8
Masseter	10	10/10	1·32 ± 0·13	13·0 ± 2·1

Values for k and duration are given as means ± S.D.

Central peaks were seen in cross-correlograms constructed from left and right masseter recordings in all subjects ($n = 10$). The duration of the peak ranged from 10 to 17 ms (mean 13·0 ms), and the amplitude, expressed in terms of k, ranged from 1·17 to 1·50 (mean 1·32 ms). Secondary features were less pronounced in these correlograms than in those observed in correlograms constructed from multiunit EMG recordings from left and right diaphragm and rectus abdominis. Secondary peaks were seen in the cross-correlograms of six out of ten subjects, an example is shown in Fig. 2*C*. The mean lag was calculated to be 31 ms (S.D. 4·8, $n = 6$) from the central peak, thus giving a mean periodicity of 32 Hz (S.D. 4·2). In three of the subjects needle recordings were obtained from left and right masseter muscles. Significant central peaks were found in cross-correlograms from three of thirteen single unit recordings (2 subjects) and from four of seven multiunit recordings (3 subjects). Mean k values were 1·5 (S.D. 0·02) for single unit and 1·27 (S.D. 0·17) for multiunit cross-correlograms.

When subjects ($n = 8$) lay supine with both legs raised, cross-correlograms constructed between multiunit EMGs from left and right rectus abdominis revealed short duration (range 9·0–16 ms, mean 12·1 ms) central peaks in all cases. The size of these peaks ranged from a k value of 1·51–3·33 (mean 2·45). Whilst a central peak was the dominant feature in the cross-correlogram, secondary peaks were also seen and were often pronounced, (Fig. 2*D*). The mean lag from the central peak was 28 ms (S.D. 2·9, $n = 8$) reflecting a periodic process of 36 Hz (S.D. 4·1, $n = 8$). Cross-correlograms constructed between the left and right spike trains obtained using needle recordings in one subject

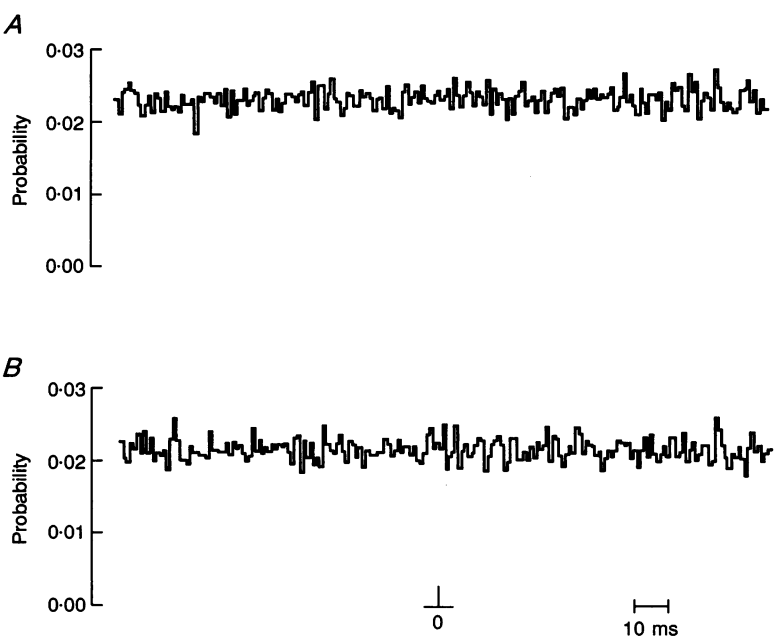

Figure 1. Cross-correlograms constructed from multiunit EMG recordings from simultaneously contracting left and right homologous muscles
In each correlogram the ordinate gives the probability of a spike in the right muscle at times before and following a spike in the left muscle. Bin width is 1 ms. 8000–10000 spikes from each spike train were used. Central peaks are not present in either correlogram. *A*, left and right FDI during a sustained index finger abduction. *B*, left and right deltoid during a sustained abduction of both arms.

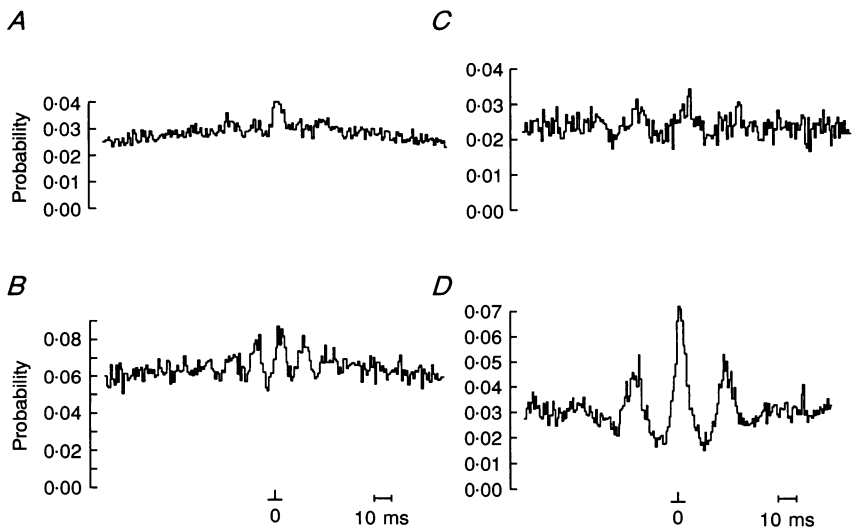

Figure 2. Cross-correlograms constructed from multiunit EMG recordings from simultaneously contracting left and right homologous muscles
In each correlogram the ordinate gives the probability of a spike in the right muscle at times before and following a spike in the left muscle. Bin width is 1 ms. 8000–10000 spikes from each spike train were used. A central peak is seen in each of these correlograms. *A* and *B*, left and right diaphragm during deep voluntarily controlled inspiration. *C*, left and right masseter whilst clenching the teeth. *D*, left and right rectus abdominis with legs raised.

also showed short duration central peaks. Correlograms constructed from single unit recordings ($n = 2$) had a mean k value of 2·6, and mean duration of 11 ms while those from multiunit recordings ($n = 7$) had a mean k value of 1·64 (S.D. 0·79) and a mean duration of 15·6 ms (S.D. 3·3).

Focal magnetic brain stimulation

Homologous left and right muscles of the upper limb

Using the stimulation sites described in Table 2, focal magnetic brain stimulation was performed whilst recording from homologous pairs of upper limb muscles. Under these conditions only contralateral short latency responses were seen (Table 4).

Threshold and size of EMG responses to magnetic stimulation

The threshold magnetic field required to evoke a response was lowest in the distal muscles of the upper limb. The latency and size of responses also showed a distal–proximal gradient. The largest responses were recorded from the FDI muscle (Fig. 3) at the longest latency and the smallest responses from the deltoid, at the shortest latency. The results of magnetic stimulation in preactivated muscles are summarized in Table 4.

Responses were easily and consistently elicited in the contralateral muscles of the upper limb. In all muscles

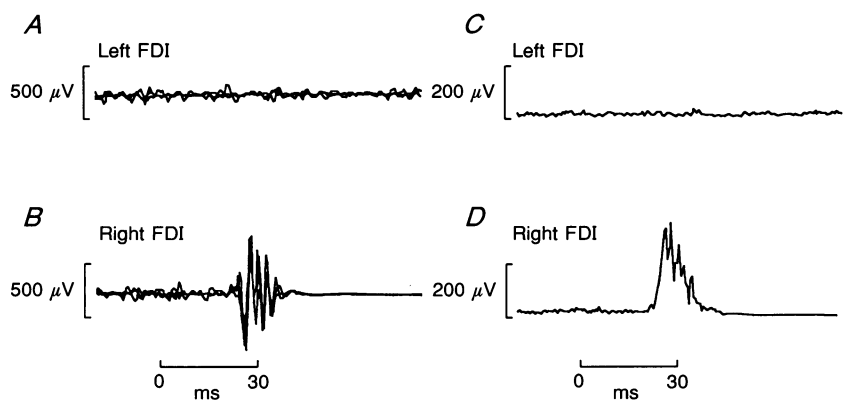

Figure 3. EMG responses recorded simultaneously from preactivated left and right FDI following focal magnetic stimulation of the left motor cortex
Stimulus occurs at time zero. *A* and *B*, 3 superimposed responses. A clear response of latency 22 ms is seen in the right muscle (*B*). No response is seen in the left muscle (*A*). *C* and *D*, average of 10 rectified responses in the same subject.

other than deltoid, it was possible to elicit responses in the relaxed muscle. When stimulating the motor cortex, without preactivation of the deltoid, it was only possible to see a response in one out of seven subjects.

Short latency, excitatory responses were never seen in the ipsilateral muscle. However, a small late increase in EMG at 45 ms was recorded from one subject in the ipsilateral deltoid muscle. This response was about 5 times smaller than the short latency excitatory response seen contralaterally at 11 ms.

When fifty to sixty responses to magnetic stimulation were averaged in two subjects, a small decrease in on-going EMG was seen ipsilaterally in the FDI and FA Ext muscles but not in ipsilateral biceps and deltoid muscles. Similar results have been described by Ferbert, Priori, Rothwell, Day, Colebatch & Marsden (1992).

Homologous left and right axial and truncal muscles

Focal magnetic stimulation of the motor cortex evoked bilateral short latency EMG responses in these homologous muscle pairs. The characteristics of these responses are shown in Table 5.

Diaphragm muscle

Following magnetic brain stimulation, bilateral short latency responses were elicited in preactivated diaphragm muscles in six of seven subjects. In one subject only small contralateral responses were seen. The scalp site used for stimulation of diaphragm overlay the site used for stimulation of biceps muscle. This makes it unlikely that the bilateral responses observed in diaphragm were due to the simultaneous stimulation of both motor cortices, since bilateral responses were never seen in biceps muscle.

Figure 4 shows the responses evoked in left and right diaphragm for one subject. Single sweeps and the average of rectified responses are shown. The latency of the response in the ipsilateral diaphragm was significantly longer than the response in the contralateral diaphragm ($P < 0{\cdot}04$, Student's paired t test, $n = 6$). If the mean normalized area of the ipsilateral response is expressed as a fraction of the mean area of the contralateral response for each subject, it was found that the area of the ipsilateral response ranged from 0·18 to 0·74 of the area of contralateral response (mean 0·42 of the contralateral). These differences were significant ($P < 0{\cdot}03$, paired t test, $n = 6$).

With the diaphragm relaxed, bilateral responses were elicited in only two subjects following magnetic stimulation. In the remaining five subjects only contralateral responses were observed.

Rectus abdominis

Bilateral short latency responses were evoked in preactivated rectus abdominis in six out of seven subjects following magnetic brain stimulation. An example is shown in Fig. 5*A* and *B*. In one subject no clear responses were seen in the rectus abdominis following stimulation using up to 80 % of the maximum available output.

There was no significant difference between the latency of the ipsilateral and contralateral responses (paired t test, $P > 0{\cdot}05$). The ipsilateral response tended to be smaller than the contralateral response but this was not significant (paired t test, $P > 0{\cdot}05$).

Table 4. Characteristics of contralateral responses in upper limb muscles following focal stimulation of the motor cortex

Muscle	n	Threshold (% stimulator output)	Latency (ms)	Normalized area
FDI	7	25 (20–30)	21·6 ± 0·8	265·5 ± 130·4
FA Ext	7	25 (20–30)	16·8 ± 0·8	260·2 ± 117·2
Biceps	7	30 (25–35)	13·0 ± 1·8	111·4 ± 198·1
Deltoid	7	35 (25–45)	12·9 ± 1·6	94·3 ± 51·6

Range in threshold is given in parentheses. Values for latency and normalized area are means ± S.D.

Table 5. Characteristics of bilateral responses to magnetic stimulation in axial and truncal muscles

		Threshold (% stimulator	Latency		Normalized area	
Muscle	n	output)	Contra	Ipsi	Contra	Ipsi
Diaphragm	6	50 (35–70)	16·9 ± 1·7	21·1 ± 1·1	89·5 ± 50·5	39·9 ± 28·2
Rectus Abd	6	45 (35–55)	19·5 ± 2·6	21·5 ± 1·6	101·5 ± 59·2	51·2 ± 22·8
Masseter	7	35 (25–50)	7·8 ± 1·1	7·7 ± 0·9	23·5 ± 23·8	12·7 ± 6·6

Threshold range is given in parentheses. Values for latency and normalized area are means ± S.D. Contra, contralateral; Ipsi, ipsilateral.

Magnetic stimulation was performed when rectus abdominis was relaxed in five subjects; bilateral responses were evoked in four subjects and the remaining subject showed only small contralateral responses.

In one subject, bilateral responses to magnetic stimulation were recorded using needle electrodes in left and right rectus abdominis. The optimal surface site of stimulation for rectus abdominis was near the mid-line in these experiments (see Methods) and it might be argued that the bilateral responses were due to the simultaneous stimulation of both cortices. However, during the multiunit needle recording in one subject, the coil position was moved from the optimal site of stimulation (2 cm posterior and 0·7 cm lateral to Cz in this subject) to 2·5 cm lateral to Cz. Bilateral responses were again consistently elicited in rectus abdominis muscles. In the same subject stimulation at 2 cm lateral to Cz had elicited only contralateral responses in deltoid muscle. It is therefore unlikely that the bilateral responses in rectus abdominis were due to stimulus spread.

Masseter

Magnetic stimulation evoked bilateral responses in preactivated masseter muscle in all seven subjects. The standard procedure of stimulation at threshold +10 % and analysis of five sweeps was not suitable for this muscle since stimulation often led to direct excitation of the trigeminal and/or facial motor nerves ipsilaterally. Direct motor nerve excitation resulted in a short latency response (around 3 ms) in the ipsilateral masseter and tended to obscure any later cortically evoked response on that side. Thus magnetic stimulation was performed at around

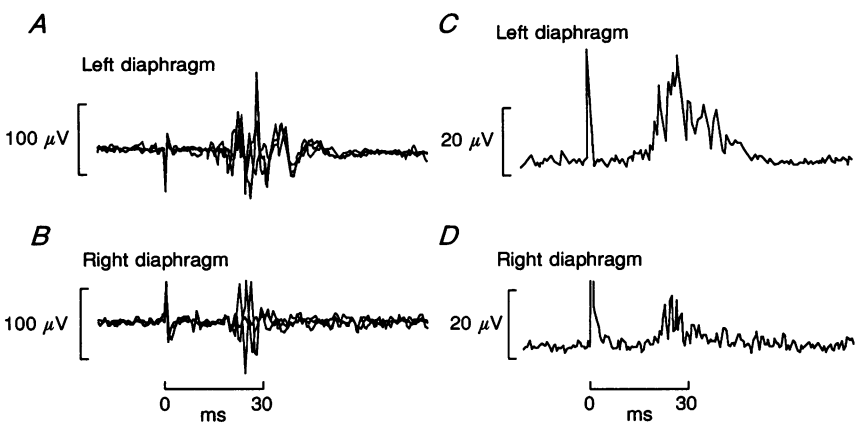

Figure 4. EMG responses recorded simultaneously from preactivated left and right diaphragm following focal magnetic brain stimulation of the right motor cortex
A and *B*, 3 superimposed responses. *C* and *D*, average of 7 rectified responses. The response in the muscle ipsilateral to the stimulus is significantly smaller than the contralateral response.

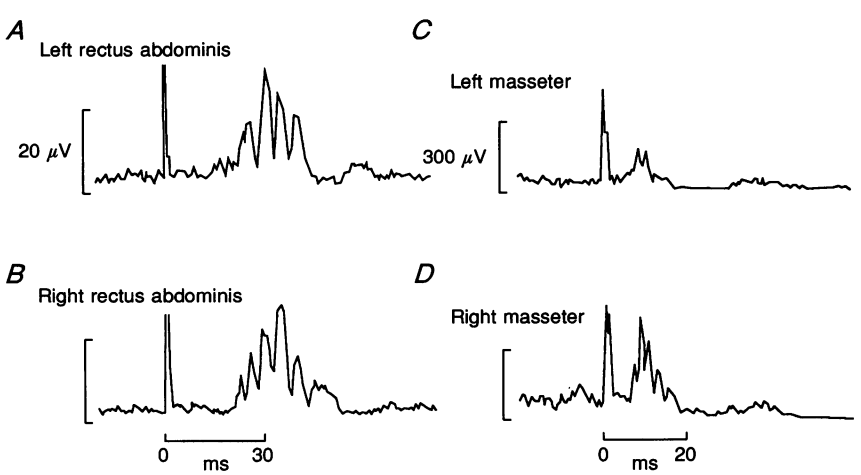

Figure 5. EMG responses recorded simultaneously from preactivated left and right homologous muscles following focal magnetic stimulation of the left motor cortex
A and *B*, average of 10 rectified responses in rectus abdominus; the ipsilateral and contralateral responses are of similar size. *C* and *D*, average of 12 rectified responses in masseter.

threshold and a larger number of sweeps were analysed (from 25 to 150). The results of stimulation in one subject are shown in Fig. 5*C* and *D*.

The latency of the ipsilateral response was not significantly different to the latency of the contralateral response in masseter (paired t test, $P > 0{\cdot}05$, $n = 7$). The ipsilateral response tended to be smaller than the contralateral response but this was not significant (paired t test, $P > 0{\cdot}05$, $n = 7$).

DISCUSSION

Two major results emerge from the present study. Firstly, cross-correlation analysis of multiunit recordings from co-activated homologous axial muscle pairs (left and right diaphragm, rectus abdominis and masseter) revealed the presence of a common drive to the motoneurone pools of the co-contracting muscle pairs. In contrast, there was no evidence for a common drive to the motoneurone pools of co-activated homologous muscle pairs of the upper limb (FDI, FA Ext, biceps and deltoid). Secondly, it was shown that unilateral magnetic brain stimulation evoked bilateral responses in axial muscles but only contralateral responses in upper limb muscles. The possible neural pathways responsible for these effects and the functional implications of activity in these pathways will now be discussed.

Homologous muscles of the upper limb

Cross-correlation analysis

No short duration central peaks were seen in cross-correlograms constructed from multiunit recordings of simultaneous activity in left and right upper limb muscles. This lack of a common drive to these co-contracting muscles is presumably commensurate with the independent control of the two arms by the central nervous system.

Focal magnetic brain stimulation

Focal magnetic cortical stimulation allows investigation of the laterality of corticospinal projections in man. In the present study, contralateral responses were recorded from FDI, FA Ext, biceps and deltoid. The short latency of these responses is consistent with the presence of a monosynaptic corticomotoneuronal projection. The size of the responses showed a distal-to-proximal gradient, being larger in the more distal muscles. A similar finding has recently been reported by Palmer & Ashby (1992). These differences in the size of the response may be explained by differences in the strength of the corticomotoneuronal projection. Indeed, in the monkey direct corticomotoneuronal connections are more numerous to distal forelimb muscles (Phillips & Porter, 1964). However, Colebatch, Rothwell, Day, Thompson & Marsden (1990) reported that responses to magnetic stimulation recorded from the deltoid muscle were of similar size to those recorded from an intrinsic hand muscle, suggesting that in man, the corticomotoneuronal projection to this proximal muscle may be as strong as that to a distal muscle.

Anatomical data and studies of patients with unilateral cortical damage suggest that the ipsilateral corticospinal tract may play some part in the control of the proximal muscles of the upper limb, for example biceps and deltoid (Brinkman & Kuypers, 1973; Colebatch & Gandevia, 1989; Benecke, Meyer & Freund, 1991). In the present study, no short latency ipsilateral excitatory responses were observed following unilateral magnetic stimulation. Thus, in healthy subjects we found no evidence for an ipsilateral, rapidly conducting, monosynaptic projection to motoneurones of proximal arm muscles. However, in one subject, a small ipsilateral response was recorded from the deltoid muscle presumably corresponding to the medium latency ipsilateral response described by Colebatch *et al.* (1990).

Homologous left and right axial and truncal muscle

Cross-correlation analysis

A short duration central peak was the most prominent feature in cross-correlograms constructed from motor units recorded from left and right diaphragm, rectus abdominis and masseter. The theoretical analysis of the central peak in a correlogram by Sears and his colleagues (Sears & Stagg, 1976; Kirkwood & Sears, 1978) provides evidence that such a peak may result from activity in branched last-order presynaptic fibres. More recently, Kirkwood & Sears (1991) have emphasized that only the narrowest of central peaks can confidently be attributed to activity in last-order branched fibres and now believe that most peaks contain a contribution from presynaptic synchronization. In the anaesthetized cat, they found that cross-correlograms constructed from the discharges of internal and external intercostal motoneurones have short duration central peaks even though the drive to the external motoneurones is more indirect than to the internal motoneurones. They conclude that synchronization of intercostal motoneurones can be produced not only by activity in branched last-order inputs to motoneurones but also if the projection of this branched input is indirect via last-order interneurones. In the present study, correlograms were constructed from multiunit EMG data. This will result in a dispersion of the central peak due to variable central and peripheral conduction delays (see Sears & Stagg, 1976; Farmer, Harrison, Ingram & Stephens, 1991). Bremner *et al.* (1991) reported that the modal value of the duration of the central peaks in their cross-correlograms constructed between single motor discharges recorded within FDI muscle was 13 ms. These authors found that the time course of such peaks could be fitted by the equations of Kirkwood & Sears (1978). Hence, mean durations of 11·3–13·0 ms, as seen in this study could well be consistent with the

hypothesis that they result from activity in last-order branched fibres. Nevertheless, in the present study, taking into account the work of Kirkwood & Sears (1991), it seems likely that presynaptic synchronization also contributes to the central peak of the correlograms.

Periodicities may be present in a correlogram, making interpretation of the correlogram more difficult. In the present study, periodicities were present in all correlograms constructed from recordings from left and right diaphragm; these were seen as peaks of decreasing amplitude either side of the central peak. All correlograms from left and right rectus abdominis had secondary peaks while just over half of those from left and right masseter had these peaks. One interpretation of secondary peaks is that they could reflect the firing frequency of the common input (Moore, Segundo, Perkel & Levitan, 1970) if this input is periodic. For the rectus abdominis and masseter muscles, this would suggest mean firing rates of 36 and 32 Hz respectively for the common drive. This is at the upper end of those rates seen by Bremner *et al.* (1991) when analysing the secondary peaks seen in correlograms constructed from single units recorded from intrinsic hand muscles. In the present study, assuming that activity in corticospinal fibres contributed to the features of the correlograms, periodic activity of the common input could result from synchronization of cortical cells. Such synchronization has been described previously (Allum, Hepp-Reymond & Gysin, 1982; Smith & Fetz, 1989) and may contribute to muscle synergies (Kang, Endo & Araki, 1991). In addition, synchronous 25–35 Hz oscillations have been reported between units in the precentral gyri of awake monkeys (Murthy & Fetz, 1991).

In correlograms constructed from units recorded from right and left diaphragm, the periodicities were in the frequency range 55–80 Hz; this type of synchronization is probably equivalent to the high-frequency oscillation (HFO) synchronization described by Kirkwood, Sears, Tuck & Westgaard (1982*a*). These authors suggest that presynaptic synchronization of medullary bulbospinal neurones, projecting to left and right phrenic motoneurones, is the most likely source of this HFO synchronization. This presynaptic synchronization will contribute to the central peak but Kirkwood *et al.* (1982*b*) concluded that in their correlograms, the central peaks also contained a component attributable to activity in last-order branched fibres. We feel that this may also be the case in our study since the central peak was the dominant feature of each correlogram.

Focal magnetic brain stimulation

Focal magnetic brain stimulation produced short latency EMG responses in both the left and right diaphragm, rectus abdominis and masseter muscles. These bilateral responses are unlikely to be the result of stimulus spread at the cortical level (see Results); hence our results suggest a direct, or relatively direct, projection from the motor cortex to these homologous muscle pairs. Such responses have previously been reported for the diaphragm (Gandevia & Rothwell, 1987; Maskill *et al.* 1991) rectus abdominis (Plassman & Gandevia, 1989; Cohen, Bandinelli, Topka, Fuhr, Roth & Hallet, 1991) and masseter (Benecke, Meyer, Schonle & Conrad, 1988; Cruccu, Berardelli, Inghilleri & Manfredi, 1989).

The contralateral response recorded from the diaphragm was of a significant shorter latency and larger than the ipsilateral response. The bilateral pathway from cortex to diaphragm could be direct or indirect via the medulla. There is evidence in the animal literature for both pathways. Rickard-Bell, Tork & Bystrzycka demonstrated in 1986, using anterograde tracing, that corticospinal axons in the cat do project directly to phrenic motoneurones. The projection was mainly contralateral but some fibres were seen to recross the spinal cord and supply the ipsilateral motoneurone pool. Although the shortest latency at which a response was seen was significantly shorter in the contralateral muscle, visual inspection of the responses reveals that the major part of both the ipsi- and contralateral responses occurs at about the same time. Hence, perhaps the same pathway is involved in producing both responses but that projecting contralaterally contains some faster fibres.

Alternatively, the ipsilateral response may have resulted from activity in corticospinal fibres that excite bilaterally projecting brainstem pathways. The earliest components of the contralateral response may arise from direct corticospinal excitation while later components may result from bulbospinal excitation and repetitive firing of corticospinal neurones.

Whatever the mechanism, the ipsilateral response was always significantly smaller than the contralateral response suggesting that the ipsilateral projection is sparse.

Common drive to axial muscles

Cross-correlation analysis suggests that the left and right diaphragm, rectus abdominis and masseter muscles each share a common drive. As argued above, this drive probably comprises activity in last-order branched fibres and presynaptic synchronization. Focal magnetic stimulation of the motor cortex produced bilateral responses in these homologous muscle pairs.

For the rectus abdominis and masseter muscle pairs, the latencies and sizes of these ipsilateral and contralateral responses were not significantly different. Taken together with the results of the cross-correlation analysis for these two muscle pairs, the results suggest that corticospinal fibres may provide the common drive to the left and right motoneurone pools.

This common drive may arise from activity in corticospinal fibres that branch and supply the left and right motoneurone pools and from activity in corticospinal tract

cells whose activity is synchronized at the cortical level.

Although our results suggest that the corticospinal tract may innervate both left and right phrenic motoneurone pools, it is difficult to assess the contribution of activity in these axons to the central peak of the correlograms. Kirkwood *et al.* (1982*a*) concluded that bulbospinal axons were responsible for the synchronization between intercostal motoneurones. Using electrophysiological and histological techniques, Rikard-Bell, Bystrzycka & Nail (1985) demonstrated that in the cat brainstem, neurones of both the dorsal and ventral respiratory group project bilaterally to respiratory motoneurones. Some of these connections are monosynaptic (Davies, Kirkwood & Sears, 1985; Duffin & Lipski, 1987). It therefore seems highly likely that this bulbospinal input also contributed to the correlogram features in the present study. However, in the present study, respiration was being controlled voluntarily and under these conditions one would expect some cortical involvement (Colebatch *et al.* 1991). Furthermore, Adams, Datta & Guz (1989) showed that for an accessory muscle, the sternocleidomastoid, the amount of synchrony between motoneurones was greater during voluntary controlled breathing than during reflex breathing. Finally, Kirkwood *et al.* (1982*a*) found that HFO and short-term synchronization became more apparent, while broad peak synchronization was reduced, if the CO_2 level was increased; these authors attributed this to an increase in output from the midbrain respiratory centres. In our study, since subjects were breathing deeply, the CO_2 level must surely have been reduced (some subjects reported dizziness) and presumably so was the respiratory drive from the midbrain. Hence, it seems likely that activity in corticospinal and bulbospinal pathways must have contributed to the correlogram features in the present study.

Functional implications of results

It has been observed that following a unilateral cerebrovascular accident in man, motor function is usually preserved in the muscles of respiration, trunk movement and mastication, whereas profound weakness is often seen in distal muscles (Broadbent, 1866; Willoughby & Anderson, 1984; Colebatch & Gandevia, 1989). This pattern suggests that the motor cortex provides strong ipsilateral corticospinal projections to muscles which act symmetrically. The findings of the present study would support and explain these observations.

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